B5 cont.

casein; non-reduced samples. Amount of sample applied corresponding to 0.4 mg and 4.5 mg of skin for Tg and Wt, respectively. Arrow denotes SCCE.

IN THE CLAIMS

Please cancel claims 5-7, 14 and 19.

Please amend claims 1, 2, 4, 8-13, 15-18, 20-30 to read as follows:

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1 (amended). A non human transgenic mammal which is a rodent selected from the group consisting of mice, rats and rabbits, having integrated within its genome a nucleotide sequence comprising (1) a heterologous nucleotide sequence coding for a stratum corneum chymotryptic enzyme (SCCE) which hybridizes with the complementary sequence to the nucleotide sequence SEQ ID NO:1 under stringent hybridization conditions, or (2) a heterologous nucleotide sequence which encodes the same amino acid sequence as that encoded by the heterologous nucleotide sequence of (1), operably linked to a ubiquitous promoter that drives expression of said heterologous *scce* in skin.

2 (amended). A non human transgenic mammal according to claim 1 wherein said operably linked ubiquitous promoter drives expression of *scce* in epidermis.

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4 (amended). A non human transgenic mammal according to claim 1 having integrated within its genome a heterologous nucleotide sequence comprising a nucleotide sequence coding for a protein, having serine protease activity, with an amino acid sequence which has a sequence identity of at least 75% to the amino acid sequence shown in SEQ ID NO:2 and which comprises the partial sequence X_3-asparagine-X_4-X_5-X_6 X_7-X_8-serine shown in SEQ ID NO:15, wherein X_3 is any amino acid residue, X_4 is any amino acid residue, X_5 is a cystein residue X_6 is any amino acid, X_7 is

B7 cont. a glycine residue, X_8 is an aspartate residue, and the serine is the active serine residue characteristic of serine proteases, operably linked to a ubiquitous promoter that drives expression in skin.

8 (amended). A non-human transgenic mammal according to claim 1 which is a mouse.

9 (amended). A non human transgenic mammal according to claim 1, wherein the nucleotide sequence comprises a DNA sequence coding for human SCCE as shown in SEQ ID NO:1.

B8 10 (amended). A non human transgenic mammal according to claim 1, wherein the nucleotide sequence codes for the peptide shown in SEQ ID NO. 2.

11 (amended). A non human transgenic mammal according to claim 10, wherein the DNA sequence codes for the peptide corresponding to amino acid no. 23 through no. 253 of the amino acid sequence shown in SEQ ID NO. 2.

12 (amended). A non human transgenic mammal according to claim 10, wherein the DNA sequence codes for the peptide corresponding to amino acid no. 30 through no. 253 of the amino acid sequence shown in SEQ ID NO. 2.

13 (amended). A non human transgenic mammal according to claim 1, wherein the DNA sequence codes for the peptide shown in SEQ ID NO. 2.

15 (amended). A non-human transgenic mammal according to claim 1, wherein the heterologous nucleotide sequence is SEQ ID NO:1.

B9 16 (amended). A non-human transgenic mammal according to claim 1, wherein the promoter is a heterologous promoter.

17 (amended). A non-human transgenic mammal according to claim 16, wherein the promoter is an SV40 promoter.

18 (amended). A non-human transgenic mammal according to claim 17, wherein the promoter is the SV40 early promoter.

20 (amended). A non-human mammal according to claim 1, wherein the mammal exhibits an abnormal skin phenotype.

21 (amended). A non-human mammal according to claim 1, wherein the mammal exhibits predisposition for cancer.

22 (amended). A non-human mammal according to claim 21, wherein the mammal exhibits a predisposition for ovarian cancer.

23 (amended). A non-human mammal according to claim 20, wherein the mammal exhibits an abnormal skin phenotype resembling a skin disease.

24 (amended). A non human mammal according to claim 23, wherein the mammal exhibits epidermal hyperkeratosis, achantosis, epidermal and/or dermal inflammation and/or pruritus.

B10

25 (amended). A non human mammal according to claim 24, wherein the mammal exhibits an abnormal skin phenotype resembling inflammatory skin diseases selected from the group of diseases consisting of epidermal hyperkeratosis, acanthosis, epidermal inflammation, dermal inflammation and pruritus.

26 (amended). A non-human mammal according to claim 23, wherein the mammal exhibits an abnormal skin phenotype resembling psoriasis.

27 (amended). A non human mammal according to claim 23, wherein the mammal exhibits an abnormal skin phenotype resembling chronic atopic dermatitis or chronic eczema.

28 (amended). A non-human mammal according to claim 23, wherein the mammal exhibits an abnormal skin phenotype resembling inherited skin diseases with epidermal hyperkeratosis.

29 (amended). A method for making a transgenic non human mammal, which is a rodent selected from the group consisting of mice, rats and rabbits, having integrated within its genome a nucleotide sequence construct comprising (1) a heterologous nucleotide sequence coding for a stratum corneum chymotryptic enzyme (SCCE) and which hybridizes with the complementary

sequence to the nucleotide sequence SEQ ID NO:1 under stringent hybridization conditions, or (2) a heterologous nucleotide sequence which encodes the same amino acid sequence as that encoded by the heterologous nucleotide sequence of (1), operably linked to a ubiquitous promoter that drives expression of *scce* in skin, the method comprising

(a) constructing and amplifying said heterologous nucleotide sequence construct,

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(b) introducing said heterologous nucleotide construct into a non-human cell from a rodent selected from the group consisting of mice, rats and rabbits,

(c) using said cell or the progeny of said cell to create a number of putative transgenic non-human mammals, and

(d) selecting said non-human mammal having said heterologous nucleotide construct integrated within its genome.

30 (amended). A method for making a transgenic non-human mammal according to claim 29 wherein said operably linked ubiquitous promoter drives expression of *scce* in epidermis.

Please add the following new claims:

59 (new). A non human transgenic mammal which is a rodent selected from the group consisting of mice, rats and rabbits, having integrated within its genome a nucleotide sequence comprising (1) a heterologous nucleotide sequence of a

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heterologous stratum corneum chymotryptic enzyme (SCCE) gene, which hybridizes with the complementary sequence to the nucleotide sequence SEQ ID NO:3 under stringent hybridization conditions, or (2) a heterologous nucleotide sequence which encodes the same amino acid sequence as that encoded by the

heterologous nucleotide sequence of (1), operably linked to a ubiquitous promoter that drives expression of said heterologous sequence in skin.

60 (new). The mammal of claim 1 in which the promoter is selected from the group consisting of SV40 promoter, polyoma early promoter, retroviral long terminal repeats (5'-LTR), adenovirus promoters, β-actin promoter, and ribosomal protein promoters.

61 (new). The mammal of claim 4 in which the promoter is selected from the group consisting of SV40 promoter, polyoma early promoter, retroviral long terminal repeats (5'-LTR), adenovirus promoters, β-actin promoter, and ribosomal protein promoters.

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62 (new). The mammal of claim 59 in which the promoter is selected from the group consisting of SV40 promoter, polyoma early promoter, retroviral long terminal repeats (5'-LTR), adenovirus promoters, β-actin promoter, and ribosomal protein promoters.

63 (new). The mammal of claim 4 in which the promoter is the SV40 early promoter.

64 (new). The mammal of claim 59 in which the promoter is the SV40 early promoter.

65 (new). The mammal of claim 1 in which clause (1) applies.

66 (new). The mammal of claim 59 in which clause (1) applies.

67 (new). The mammal of claim 4 in which the sequence identity is at least 80%.

68 (new). The mammal of claim 4 in which the sequence identity is at least 90%.

69 (new). The mammal of claim 4 in which the sequence identity is at least 95%.